The Swiss Canine Cancer Registry: a retrospective study on the occurrence of tumours in dogs in Switzerland from 1955 to 2008

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Abstract: Diagnostic records are a key feature of any cancer epidemiology, prevention or control strategy for both human beings and animals. Thus, the information stored in human and animal cancer registries is essential to comparative epidemiologic, pathogenic and therapeutic research.
This study presents the Swiss Canine Cancer Registry, compiled between 1955 and 2008. The data consists of pathology diagnostic records issued by three veterinary diagnostic laboratories in Switzerland. The tumours are classified according to the International Classification of Oncology for Humans (ICD-O-3) guidelines: tumour type, malignancy and body location (WHO, 2013). The dogs are classified according to breed, age, sex, castration status and place of residence.
The diagnostic data were correlated to the relative dog population and the occurrence of cancer in dogs was thus investigated. In 121,963 canine patients 67,943 tumours were diagnosed. 47.07% of which were malignant tumours. The most common tumour location was the skin (37.05%), followed by mammary glands (23.55%) and soft tissue (13.66%). The most common tumour diagnoses were epithelial (38.45%), mesenchymal (35.10%) and lymphatic tumours (13.23%).
The results are compared with other canine registries. Similarities to tumour distribution and incidence in other findings are listed and specific difficulties in comparison are pointed out. We hope that this study will mark the beginning of a continuous registration of dog tumours in Switzerland, which, in turn, will serve as a reference for research in the fields of animal and human oncology.

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Dear Editor

Enclosed you will find a manuscript entitled: „The Swiss Canine Cancer Registry: a retrospective study on the occurrence of tumours in dogs in Switzerland from 1955 – 2008" by K.Grüntzig[2], R. Graf[2], M. Hässig[3], M. Welle[9], D. Meier[8], G.Lott[1], D. Erni[7], N.S. Schenker[1], F. Guscetti[1], G. Boo[5], K. Axhausen[6,2], S. Fabrikant[5], G. Folkers[2] and A. Pospischil[1,2] from [1]Institut für Veterinärpathologie Universität Zürich, [2]Collegium Helveticum, Universität Zürich und Eidgenössische Technische Hochschule Zürich (ETHZ), [3]Departement Nutztiere, Universität Zürich, [4]Kantonales Veterinäramt Zürich, [5]Geographisches Institut, Universität Zürich, [6]Institut für Verkehrsplanung und Transportsysteme (IVT), ETHZ, [7]FocusedPublishing GmbH, CH-8332 Russikon, [8]Zyto-Histo Diagnostics and [9]Institut für Tierpathologie Universität Bern I would greatly appreciate a review and a publcation as full length paper.

Best regards

Andreas Pospischil

The Swiss Canine Cancer Registry: a retrospective study on the occurrence of tumours in dogs in Switzerland from 1955 – 2008

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Summary

Diagnostic records are a key feature of any cancer epidemiology, prevention or control strategy for both human beings and animals. Thus, the information stored in human and animal cancer registries is essential to comparative epidemiologic, pathogenic and therapeutic research.

This study presents the Swiss Canine Cancer Registry, compiled between 1955 and 2008. The data consists of pathology diagnostic records issued by three veterinary diagnostic laboratories in Switzerland. The tumours are classified according to the International Classification of Oncology for Humans (ICD-O-3) guidelines: tumour type, malignancy and body location (WHO, 2013). The dogs are classified according to breed, age, sex, castration status and place of residence.

The diagnostic data were correlated to the relative dog population and the occurrence of cancer in dogs was thus investigated. In 121,963 canine patients 67,943 tumours were diagnosed. 47.07% of which were malignant tumours. The most common tumour location was the skin (37.05%), followed by mammary glands (23.55%) and soft tissue (13.66%). The most common tumour diagnoses were epithelial (38.45%), mesenchymal (35.10%) and lymphatic tumours (13.23%).

The results are compared with other canine registries. Similarities to tumour distribution and incidence in other findings are listed and specific difficulties in comparison are pointed out. We hope that this study will mark the beginning of a continuous registration of dog tumours in Switzerland, which, in turn, will serve as a reference for research in the fields of animal and human oncology.

Keywords: canine, cancer, registry, epidemiology, tumour

Introduction

Cancer is a leading cause of death in both humans and dogs (Pinho et al., 2012). However, current medical research is hampered by the complex biology of the disease. Murine cancer models are highly standardised experiments which have contributed tremendously to knowledge about cancer mechanisms and treatment regimes. Nonetheless, murine cancer models are frequently limited in representing specific aspects of spontaneous human cancer such as long time latency, recurrence and metastasis (Porello et al., 2006; Thamm and Dow, 2009; Martić-Kehl et al., 2012; Ranieri et al., 2013).

To fill in the knowledge gaps of spontaneous cancer models, cancer registries provide a key to the epidemiology of cancer over space and time. In many industrial countries, human cancer registration has been an established practice since the 1940s (Brønden et al., 2007). Companion animal cancer registries were introduced in the 1960s, following increasing mortality due to spontaneous tumours. The study of companion animal tumours offers several benefits not only for animal epidemiology but also for comparative epidemiologic, pathogenic and therapeutic research. Companion animals have a functioning immune system and a length of life span that allow them to develop tumours resembling human tumours in morphology and behaviour. Companion animals also benefit from oncologic therapies that are commonly applied to humans. Companion animals share the same habitat conditions as their caregivers and can thus indicate environmental hazards (Bukowski and Wartenberg, 1997; Backer et al., 2001; Gamlen et al., 2008; Marconato et al., 2009; Bettini et al., 2010). Companion animals, and dogs in particular, share significantly more genes with humans than do rodents (Pinho et al., 2012). Therefore investigations of spontaneous dog cancer can provide a partial alternative to animal testing (Bukowski and Wartenberg, 1997; Thamm and Dow, 2009).

In the 1960s and 1970s three population-based animal registries were completed in the USA: the California Animal Neoplasm Registry (1963 - 1966) (Dorn, 1968), the Kansas University Neoplasm Registry (1961 - 1971) (Strafuss, 1976) and the Tulsa Registry of Canine and Feline Neoplasms (1972 - 1977) (MacVean et al., 1978). Since the late 1980s several animal cancer registries have been established and are still being updated: the Purdue Comparative Oncology Program (since 1979) (Purdue Comparative Oncology Program, 2006), the Cancer Registry and Surveillance System for Companion Animals, Cornell (since 1980) (Page, 2004), the Animal

Tumour Registry of Genoa (since 1985) (Merlo et al., 2008), the Norwegian Cancer Project (since 1990) (Gamlen et al., 2008), the VetCancer Registry (since 1994) (Brønden et al., 2007), the Registry on Canine Tumours in Sweden/Agria (since 1995) (Egenvall et al., 2011), the Danish Veterinary Cancer Registry (since 2005) (Brønden et al., 2010), the Animal Tumour Registry of the Vicenza and Venice provinces (since 2009) (Vascellari et al., 2009) and the Guelph Companion Animal Cancer Epidemiologic Registry (since 2010) (Nødtvedt et al., 2011).

The Swiss Canine Cancer Registry (1955 - 2008) has been assembled as part of the project “One Medicine - One Oncology: Incidence and geographic distribution of companion animal cancer in Switzerland 1955 - 2008”. Additionally, the project benefits from information about the population at risk, since the chipping and registration of dogs in Switzerland has been compulsory since 2006. The dog population was surveyed with an accuracy reaching 95% in 2008 (personal information, Gesellschaft für Schweizer Tierärzte, the Swiss Society of Veterinarians). These latest data, together with data originating from previous research on the dog population, allows linking our results to the total population of dogs in Switzerland (Pospischil et al., 2013).

The aim of this paper is to present the Swiss Canine Cancer Registry, which was compiled between 1955 and 2008. Data consists of pathology diagnostic records issued by three veterinary diagnostic laboratories in Switzerland. The tumours are classified according to the International Classification of Oncology for Humans (ICD-O-3) guidelines: tumour type, malignancy and body location (WHO, 2013). The dogs are classified according to breed, age, sex, castration status and place of residence. The analysis provides a retrospective overview of the frequency of malignant and benign neoplasms. We also relate these findings to the general dog population and characterize the distribution of tumours by type, behaviour, body location, age and diagnostic method.

Material and methods

Data source

This study is based on a dog tumour registry comprising 121,963 diagnostic records of dog patients provided by three veterinary diagnostic laboratories in Switzerland: the Vetsuisse Faculty Institut für Veterinärpathologie Zürich (IVPZ), Institut für Tierpathologie Bern (ITP) and the Zyto-Histo Diagnostics private veterinary diagnostic laboratory (based in Rorbas Freienstein).

IVPZ (1955 – 2008): Three sets of diagnostic records (n=97,759) from canine post-mortem, biopsy and cytology samples. The sets originate from three time periods:

- IVPZ-GL (1955 - 1964): Set of diagnostic records (n=3,797) from canine post-mortem samples. The records were originally handwritten documents and later digitized in an Excel file.
- IVPZ-SLK (1964 - 1988): Set of diagnostic records (n=33,100) from canine post-mortem and biopsy samples. The records were transcribed to punch cards using diagnostic key words (Keydex, Fa. Royal McBee; Stünzi and Lott-Stolz, 1967). These records were digitized by Scydoc, an external company based in Zug, Switzerland. The results were crosschecked using the original typed reports.
- IVPZ-APPX (1987 - 2008): Set of diagnostic records (n=60,862) from canine post-mortem, biopsy and cytology samples. The records were stored in the electronic patient record system of the IVPZ. In 1987 when the digitized collection of data started, the punch cards were still used. There was no overlapping of data since patients were only recorded in one of the systems.

ITP (1983 - 2008): Set of diagnostic records (n=20,674) from canine post-mortem and biopsy samples.

Zyto-Histo Diagnostics (2007 - 2008) Set of diagnostic records (n=3,530) from canine biopsy samples.

The samples from the IVPZ, ITP and Zyto-Histo Diagnostics were examined by histopathology.

Data preparation

The data sets were compiled in a FileMaker database, which was exported into a Stata database. Individual diagnostic records were standardized according to age, sex, castration status and breed. The diagnoses were then coded according to the tumour topographic and morphologic keys of the ICD-O-3 (Table 1 and Table 2) and

checked for plausibility using the original patient records. All tumour diagnoses were confirmed by histopathology. Epidermal cysts were excluded. Diagnoses were grouped for future comparison with human cancer and for this reason some of these groups may be unusual for veterinarians. The groups are described in Table 3. The term “epithelial tumour” is used in two different ways: first as an overall group including all types of epithelial tumour and then as a narrow group: “epithelial* tumour” (Table 3).

Tumour groups included malignant and benign tumours, e.g. adenoma and adenocarcinoma were categorized as one group “adenoma, adenocarcinoma”. Each diagnostic record shows information about the tumour malignancy grade in an additional field. To investigate the malignancy, the tumour group was divided into “benign” (malignancy grade 0 - 2) and “malignant” (malignancy grade 3 - 6) according to the ICD-O-3 classification. Because benign tumours can develop into malignant tumours of the same type, we did not treat tumours such as adenoma and adenocarcinoma as separate groups. The same procedure was applied to coupled tumour groups, like lymphangioma and lymphangiosarcoma, osteoma and osteosarcoma, naevi and melanoma, myxoma and myxosarcoma. As different pathologists had worked on the diagnostics, we encountered two different approaches to specifying the location of fibrosarcomas in the subcutaneous tissue. Some pathologists used “skin” as the location because of the skin biopsy. Other pathologists used “soft tissue” as the origin of the tumours. We conflated these two locations and recoded “skin” as “soft tissue” for fibrosarcomas.

Breed allocation is based on information available in the diagnostic records. A declaration of one or two mixed breeds is categorized according to the first breed. A non-specific allocation as mixed breed, bastard or crossbreed is categorized under crossbreed. The 17 most common breeds, each one comprised of more than 900 individuals, were further investigated. The remaining breeds and the diagnostic records with unknown breeds were listed as "Other breeds". The breed category Shepherd includes German Shepherd, Beauceron Berger de Beauce, White Shepherd, Berger de Picardie, Berger de Savoie, Berger des Pyrénées, Groenendael, Laekenois, Malinois, Tervueren.

Diagnostic records for dogs residing outside Switzerland were excluded from the analysis.

Results

Dataset

A total of 121,963 dogs were examined through histopathology, of which 63,214 (51.83%) were diagnosed with tumour lesions. Of those, 59,124 (93.53%) had developed a single tumour and 4,090 (6.47%) had developed multiple tumours. Furthermore, 35,232 (52.93%) of the tumours were benign and 31,336 (47.07%) malignant. The proportion of tumour bearing patients versus patients without a tumour lesion differed according to the method of examination: in biopsy histopathology 64.81% of the patients were diagnosed with a tumour lesion, in cytological examinations 41.96% and in post-mortem examinations 31.04%.

Breed distribution

Our data set refers to 182 different dog breeds (n=101,281), a large number of crossbreeds (n= 12,193) and some unclassified breeds (n=8,489). The most frequent breed was the Shepherd dog (10.13%), closely followed by Crossbreeds (10.00%) and Retriever (9.37%) (Table 4).

Incidence rates

Figure 1 shows the influence of the examination methods on the annual tumour incidence rate. Post-mortem examination had a relatively stable annual incidence rate: 13 cases of neoplasia per 100,000 dogs in 1955 and 20 cases in 2008. A peak of 65 cases per 100,000 dogs was observed in the 1980s. Conversely, the overall annual tumour incidence rate rose from 13 cases of neoplasia per 100,000 dogs in 1955 to 695 cases in 2008. This trend is comparable with the rise of the incidence rate of biopsy and cytology cases, which increased from 141 cases of neoplasia per 100,000 dogs in 1968 to 675 cases in 2008.

Distribution of the most common diagnoses

The most common tumours were epithelial (38.45%), mesenchymal (35.1%), lymphatic (13.23%), melanoma (3.90%), skeletal (1.74%) and special gonadal neoplasia (1.57%). Figure 2 presents a more detailed distribution of diagnoses, with adenoma and adenocarcinoma (32.62%) at the top.

The most prevalent diagnoses over time (1955 – 2008)

The proportion of epithelial tumours declined from 45.65% in 1955 to 34.46% in 2008, whereas the proportions of mesenchymal and lymphatic tumours, melanoma and special gonadal neoplasia rose. Mesenchymal tumours rose from 28.26% in 1955 to 34.36% in 2008, lymphatic tumours from 8.70% to 14.69%, melanoma from 0.00% to 5.18% and special gonadal neoplasia from 0.00% to 2.47% (Figure 2).

Malignancy of the most common tumour diagnoses

Of total tumours, 47.07% were malignant. The following tumour groups had malignancy rates higher than the overall rate: skeletal tumours (96.61%), melanoma (87.21%), gonadal germ cell tumours (86.38%), epithelial tumour (56.52%), lymphatic tumour (52.79%). The following tumour groups had malignancy rates lower than the overall rate: neural tumours (43.38%), unclassified neoplasms (32.6%), mesenchymal tumours (29.65%), lymphangioma and lymphangiosarcoma (16.09%), special gonadal neoplasia (8.15%) and odontogenic neoplasia (2.67%). Figure 4 presents the malignancy rate of the most frequently occurring tumour groups.

A more accurate grouping shows that the following tumour groups had malignancy rates higher than the overall rate: mesothelial neoplasia (100%), complex epithelial neoplasia (99.47%), leukaemia (99.39%), transitional cell papilloma, transitional cell carcinoma (98.21%), other neoplasia of bones (96.45%), osteoma and osteosarcoma (95.49%), glial neoplasia (94.26%), epithelial* tumour (89.97%), soft tissue sarcoma (88.24%), naevi and melanoma (87.21%), gonadal germ cell tumour (86.38%), myxoma and myxosarcoma (83.24%), plasma cell neoplasia (82.44%), synovia like neoplasia (53.49%), histiocytic neoplasia (52.13%), adenoma and adenocarcinoma (50.79%), paraganglioma (48.5%).

Location of tumours

Most of the neoplasms were located in the skin (32.29%), the mammary gland (20.53%) and the soft tissue (11.90%). Figure 5 shows that the frequency of tumours in all other locations was below 10%. The tumour locations in post-mortem samples were more balanced than in the overall data and the ranking was different (Figure 6). The gastrointestinal tract (11.40%) and the respiratory system (10.63%) were the leading tumour locations. The largest variety of tumour types was found in the mouth and the pharynx, where seven different tumour types were identified (Figure7).

Age distribution

The age distribution of canine patients (Figure 8) shows that most patients, irrespective of tumour presence, were between five and ten years old (48.79%). Another large group consisted of dogs older than ten years of age (21.42%). Only 16.80% were between one and five years old, and the group of under one year old dogs (6.84%) mainly consisted of patients without tumours.

Discussion

To our knowledge, the figures of 121,963 canine patients and 67,943 tumour diagnoses collected over 53 years renders the Swiss Canine Cancer Registry the most comprehensive animal cancer registry at a national level. However, there are some shortcomings, which are typical of long-term retrospective studies. One such issue is that diagnoses were made by different pathologists at different time periods. The criteria for certain diagnoses may have changed over time and in some cases there may be a subjective factor in histopathologic diagnostics. This problem was overcome by restricting data evaluation to such tumour entities as could be clearly identified and have been known for a long time.

The yearly distribution of breeds in the Swiss Canine Cancer Registry reflects the change in various breeds' fashion in the Swiss dog population, as described by Pospischil et al. (2013). In the 1950s and 1960s Poodle (13.80%), Shepherd (12.66%), Crossbreed (10.61%), Boxer (9.75%) and Dachshund (9.69%) were the most common breeds. From 1970 to 2008 the most common breeds were Crossbreed (10%), Retriever (9.97%), Shepherd (9.87%) and Swiss Mountain Dog (6.53%).

During the study period, the Swiss dog population increased constantly and the relative tumour incidence rose dramatically, from 13 cases per 100,000 dogs at risk in 1955 to 695 in 2008. This trend could be explained by selection bias, due to the availability of new diagnostic methods, namely biopsies (since 1968) and fine needle aspirations (since 1991). We also suppose that this trend may be influenced by a rising prevalence of tumours in dogs. In fact, similarly to humans, dogs' life expectancy has risen constantly since 1955, due to advancements in veterinary medicine. An increased life expectancy, however, makes dogs more susceptible to tumours, since tumours tend to develop at an older age (Bonnet and Egenvall, 2010). On the other hand, the tumour incidence rate in post-mortem samples did not increase over time. This might at least partly be explained by the decreasing relative number of post-mortem investigations, as dog owners tend to refuse a post-mortem examination for affective reasons. Moreover, since the introduction of biopsy, tumours may have been diagnosed before death, so that a post-mortem investigation was no longer necessary.

Additional factors that may have contributed to the increasing canine tumour incidence rate in Switzerland are the following. First, the change in dogs' role in society from working dogs to family members, fully entitled to veterinary care,

diagnostic examinations and therapeutic intervention. Second, the standard of living has generally risen over the years and dog owners can afford systematic diagnostic examinations. Third, the density of licensed veterinary practices increased from 2 practises per 100,000 dogs to 346 practises per 100,000 dogs in Switzerland, between 1955 and 2008 (personal information, Gesellschaft für Schweizer Tierärztinnen und Tierärzte, the Swiss Society of Veterinarians), democratizing veterinary care over the whole country. Fourth, the evolution of environmental risk factors (e.g. UV radiation or air pollution) may have encouraged tumour development (Porello et al., 2006; Reif and Cohen, 1979). Environmental factors responsible for dog tumours are topics to be investigated in future research.

It is generally difficult to compare tumour incidences between animal cancer registries, because of differences in the sampling methods (MacVean et al., 1978; Brønden et al., 2007; Vascellari et al., 2009; Egenvall et al., 2011; Brønden et al., 2010). In order to estimate the population at risk, a telephone survey was undertaken in Northern Italy (Vascellari et al., 2009). Data were collected from an animal health insurance company (Agria) in Sweden (Egenvall et al., 2011) or by counting the "veterinarian-using" dogs in Tulsa, USA (MacVean et al., 1978)) and by legally regulated dog registration in Denmark in the Danish Dog Registry (Brønden et al., 2010) and, since 2006, in Switzerland.

However, in Switzerland, the tumour incidence rate for 2008, which reached a value of 695 cases per 100,000 dogs, lies in a position midway between the rates of other countries. For example, 282 cases per 100,000 dogs were observed in Northern Italy (Vascellari et al., 2009), 500 cases per 100,000 dogs in Sweden (Egenvall et al., 2005), 748 cases per 100,000 dogs in the UK (Dobson et al, 2002) and 1,416 tumours per 100,000 dogs in Tulsa, USA (MacVean et al., 1978). The observed malignancy distribution (47.07%) is similar to that of other cancer registries. It was reported as 38% by Brønden et al. (2010), 50% by Gamlen et al. (2008), 49% by Merlo et al. (2008) and 51% by Vascellari et al. (2009).

Skeletal tumours and melanoma showed the highest malignancy, with 96.61% and 87.21%, respectively. These figures are also similar to the results reported by Porello et al. (2006) and Ehrhart et al. (2013). Skin (32.29%), the mammary gland (20.53%) and soft tissues (11.90%) are the most frequent tumour locations, as confirmed by Dobberstein (1937), Mulligan (1949), Dorn (1967), MacVean et al. (1978), Bastianello (1983), Arnesen et al. (2001), Dobson et al. (2002), Gamlen et al. (2008), Vascellari

et al. (2009) and Dobson (2013). These results are certainly influenced by the fact that both locations are easy to access and to observe, both for the dog's owner and the veterinarian.

The ranking of the tumour locations diagnosed in post-mortem investigations shows the highest values for the gastrointestinal tract (14.23%) and the respiratory system (10.63), including intrathoracal organs (13.28%). In the ranking of all tumours sampled through post-mortem and biopsy, the gastrointestinal tract (7.49%) and the respiratory system, including intrathoracal organs (2.09%) hold places four and six, respectively, similarly to the observations of Dobson et al. (2002), Porello et al. (2006) Vascellari et al. (2009) and Dobson (2013). The different frequencies in post-mortem samples and samples from biopsy suggest an over-reporting of tumours at easily accessible locations, together with an underestimation of impenetrable locations.

The male sexual organs rank fifth (4.43%) in all examination methods and seventh (8.45%) in the post-mortem samples. Both results demonstrate that differences depend on the method of investigation and are similar to the findings of Dobberstein (1953), Mulligan (1949), Dorn (1967) and Bastianello (1983). Vascellari et al. (2009) observe that 13.4% tumours were found in the male genital tract. In the Norwegian Canine Cancer Registry, tumours in the testes (2.4%) were less frequent than in the oral cavity (3.7%) (Gamlen et al., 2008), which is an interesting difference in the distribution of these two tumour locations compared with those in the Swiss Canine Cancer Registry. Tumours of bones, joints and joint cartilage were similar in ranking for all examination methods and post-mortem investigation, with 1.82% and 4.84%, respectively. As previously mentioned, the investigation method had a strong impact on the distribution percentage. Gamlen et al. (2008) describe tumours of bones, joints and joint cartilage as comparatively rare, with rates below 1.00%. Oral tumours amounted to 1.24% of all tumours. Vascellari et al. (2009) found oral tumours more than twice as frequently in dogs in Northern Italy (2.6%) and Gamlem et al. (2008) even more in dogs in Norway (3.7%). This discrepancy might be due to different sampling strategies. In the Swiss Canine Cancer Registry post-mortem data and biopsy samples were used, whereas in the Italian and Norwegian data biopsy samples alone were used, where an overestimation of oral tumours might be expected. In accordance with the findings of Porello et al. (2006) and Thamm and Dow (2009) oral tumours represented the highest tumour type variety, including

343 epithelial, lymphatic, mesenchymal, skeletal and odontogenic tumours and
344 melanomas. Further research on these tumours may offer important insights for
345 multi-modality therapy in clinical investigations. For the development of new
346 therapies it is advantageous that oral tumours are fast to develop and hardly
347 restrained by surgery alone (Porello et al., 2006).
348 Adenoma and adenocarcinoma were the most frequent tumours in the Swiss Canine
349 Cancer Registry, in concordance with the Tulsa Registry (MacVean et al., 1978). In
350 the Danish Veterinary Cancer Registry the most frequently observed tumours were
351 lipoma and adenoma (Brønden et al., 2010). Another study reported histiocytoma,
352 lipoma and adenoma as the most frequent neoplasia (Dobson, 2013). The assigned
353 tumour groups, however, are not always consistent, so comparison provides a rough
354 overview only.
355 We hope that this study marks the beginning of a continuous registration of dog
356 tumours in Switzerland, which will serve as reference for research in the fields of
357 animal and human oncology. To be able to compare results of different registries in
358 the future it is important that data collection is assimilated with other dog registries as
359 it is for human registries.
360
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369 **Conflict of Interest Statement**
370 The author(s) declare no potential conflicts of interest with respect to the research,
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372

373 **References**

374 ANIS 2008, www. anis.ch, [accessed 18. December 2014].

375 Arnesen K, Gamlem H, Glattre E, Grøndalen J, Moe L et al. (2001) The Norwegian
376 canine cancer register 1990–1998. Report from the project “Cancer in the dog”
377 *European Journal of Comparative Animal Practice,* **11** 159-169.

378 Backer LC, Grindem CB, Corbett WT, Cullins L, Hunter JL (2001) Pet dogs as
379 sentinels for environmental contamination. *The Science of the Total Environment,*
380 **274** 161-169.

381 Bastianello SS (1983) A survey on neoplasia in domestic species over a 40-year
382 period from 1935 to 1974 in the Republic of South Africa. VI. Tumours occurring
383 in dogs. *Onderstepoort Journal of Veterinary Research,* **50** 199-220.

384 Bettini G, Morini M, Marconato L, Marcato PS, Zini E. (2010) Association between
385 environmental dust exposure and lung cancer in dogs. *Veterinary Journal,* **186** 364-
386 369.

387 Bonnett BN, Egenvall A (2010) Age Patterns of Disease and Death in Insured
388 Swedish Dogs, Cats and Horses. *Journal of Comparative Pathology*, **142** 33–38.

389 Brønden LB, Flagstad A and Kristensen AT (2007) Veterinary cancer registries in
390 companion animal cancer: a review. *Veterinary and Comparative Oncology,* **5** 133–
391 144.

392 Brønden LB, Nielsen SS, Toft N et al. (2010) Data from the Danish Veterinary
393 Cancer Registry on the occurrence and distribution of neoplasms in dogs in
394 Denmark. *Veterinary Record*, **166** 586-590.

395 Bukowski JA, Wartenberg D. (1997) An alternative approach for investigating the
396 carcinogenicity of indoor air pollution: pets as sentinels of environmental cancer risk.
397 *Environmental Health Perspectives,* **105** 1312-1319.

398 Dobberstein J (1937) Der Krebs der Haussäugetiere. *Berliner Tierärztliche*
399 *Wochenschrift,* **7** 101.

400 Dobberstein J (1953) Zur Statistik der Geschwülste der Tieren. *Akademieverlag,*
401 *Berlin.*

402 Dobson JM, Samuel S, Milstein H, Rogers K, Wood JL (2002) Canine neoplasia in
403 the UK: estimates of incidence rates from a population of insured dogs. *Journal of*
404 *Small Animal Practice,* **43** 240-246.

405 Dobson JM (2013) Breed-Predisposition to Cancer in Pedigree-Dogs. *ISRN*
406 *Veterinary Science,* Article ID 941275.

407 Dorn CR (1967) The epidemiology of cancer in animals. *California Medicine,* **107**
408 481-489.

409 Egenvall A, Bonnett BN, Hedhammar A, Olson P (2005) Mortality in over 350,000
410 insured Swedish dogs from 1995-2000: II. Breed-specific age and survival patterns
411 and relative risk for causes of death. *Acta Veterinaria Scandinavica*, **46** 121-136.

412 Egenvall et al. (2011) Integrating databases for research on health and performance
413 in small animals and horses in the Nordic countries. *Acta Veterinaria Scandinavica*,
414 **53** 4.

415 Ehrhart NP, Stewart RD, Fan TM (2013) Tumours of the Skeletal System. *Withrow*
416 *and MacEwen's Small Animal Clinical Oncology, 5e, Withrow S.J., Vail D.M., Page R.*
417 *L., Elsevier,* 463.

418 Gamlem H, Nordstoga K, Glattre E (2008) Canine neoplasia-introductory paper.
419 *APMIS Suppl,* **125** 5-18.

420 Gesellschaft Schweizer Tierärztinnen und Tierärzte GST *http://www.gstsvs.ch,*
421 [accessed 18. December 2014].

422 MacVean DW, Monlux AW, Anderson PS, Silberg SL, Roszel JF (1978) Frequency of
423 Canine and Feline Tumours in a Defined Population. *Veterinary Pathology,* **15** 700.

424 Marconato L, Leo C, Girelli R, Salvi S, Abramo F et al. (2009) Association between
425 waste management and cancer incompanion animals. *Journal of Veterinary Internal*
426 *Medicine,* **23** 564-569.

427 Martić-Kehl MI, Schibli R, Schubiger PA (2012) Can animal data predict human
428 outcome? Problems and pitfalls of translational animal research. *European Journal of*
429 *Nuclear Medicine and Molecular Imaging,* **39** 1492-1496.

Merlo DF, Rossi L, Pellegrino C, Ceppi M, Cardellino U et al. (2008) Cancer Incidence in Pet Dogs: Findings of the Animal Tumour Registry of Genoa, Italy, *Journal of Veterinary Internal Medicine,* **22** 976-984.

Mulligan RM (1949) Neoplasms of the Dog. *The Williams and Wilkins Company.*

Nødtvedt A, Berke O, Bonnett BN and Brønden L (2011) Current status of canine cancer registration – report from an international workshop, *Veterinary and Comparative Oncology*, DOI: 10.1111/j.1476-5829.

Pinho SS, Carvalho S, Cabral J, Reis CA, Gärtner F. (2012) Canine tumors: a spontaneous animal model of human carcinogenesis. *Translational Research,* **159** 165-172.

Porello A, Cardelli P, Spugnini E P (2006) Oncology of Companion Animals as a Model for Humans. An Overview of Tumour Histotypes. *Journal of Experimental and Clinical Cancer Research*, **25** 1.

Pospischil A, Hässig M, Vogel R, Salvini MM, Fabrikant S et al. (2013) Hundepopulation und Hunderassen in der Schweiz von 1955 bis 2008. *Schweizer Archiv für Tierheilkunde,* **155** 219-228.

Page RL (2004) Summary of Cancer Surveillance and Registry Project from the Cornell University.College of Veterinary Medicine, http://envirocancer.cornell.edu/research/animalreg/summarycompanion.pdf, [accessed 18. December 2014].

Purdue Comparative Oncology Program (2006) *http://www.vet.purdue.edu/pcop/videos/index.php,* [accessed 18. December 2014].

Ranieri G, Gadaleta CD, Patruno R, Zizzo N, Daidone MG et al. (2013) A model of study for human cancer: Spontaneous occurring tumors in dogs. Biological features and translation for new anticancer therapies. *Critical Revues in Oncology/Hematology,* **88** 187-97

Reif JS, Cohen D (1979) Canine Pulmonary Disease: A Spontaneous Model for Environmental Epidemiology. *Animals as Monitors of Environmental Pollutants. Office of Publications National Acadamy of Sciences Washington, D.C., ISBN 0-309-*

02871-X, 241-252.

Strafuss AC. (1976) Sebaceous gland adenomas in dogs. *Journal of American Veterinary Medical Association*, **169** 640-642.

Stünzi H, Lott-Stolz G (1967) [Use of punch cards in veterinary pathology]. *Deutsche Tierärztliche Wochenschrift*, **74** 182-184.

Thamm D and Dow S (2009) How companion animals contribute to the fight against cancer in humans. *Veterinaria Italiana*, **45** 111□120.

Vascellari M, Baioni E, Ru G, Carminato A, Mutinelli F. (2009) Animal tumour registry of two provinces in northern italy: incidence of spontaneous tumours in dogs and cats. BioMedCentral BMC Veterinary Research, **5** 39.

World Health Organization (2013) International Classification of Diseases for Oncology (ICD-O). *WHO Press. Third Edition. First Revision.* ISBN-13 9789241548496

Table 1: Coding and grading of tumour diagnoses according to ICD-O-3.

Diagnosis	ICD-O code
Odontogenic neoplasia	ICD-O 9270 - 9330
Trophoblastic tumours	ICD-O 9104
Epithelial tumour	ICD-O 8010 - 8587, ICD-O 9050 - 9058
Germ cell tumour	ICD-O 9060 - 9085
Lymphangioma, lymphangiosarcoma	ICD-O 9590 - 9960
Lymphatic tumour	ICD-O 9590 - 9960
Melanoma	ICD-O 8720 - 8730
Mesenchymal tumour	ICD-O 8680 - 8711, ICD-O 8800 - 9040, ICD-O 9120 - 9150, ICD-O 9580
Skeletal tumour	ICD-O 9180 - 9262
Neural tumour	ICD-O 9380 - 9570
Special gonadal neoplasia	ICD-O 8610 - 8670
Unspecified tumours	ICD-O 8000

Table 2: Coding of tumour locations according to ICD-O-3.

Location	ICD-O C code
Blood, haematopoietic system	ICD-O C 42
Neoplasia of bones, joints, cartilage	ICD-O C 40 – 41
Brain, meninges, other parts of CNS	ICD-O C 70 - 72
Mammary gland	ICD-O C 50
Endocrine gland	ICD-O C 73 - 75
Gastrointestinal tract	ICD-O C 16 - 26.8
Lymph nodes	ICD-O C 77
Male sexual organs	ICD-O C 60 - 63.2
Oral cavity, pharynx	ICD-O C 2.9 - 11
Other female sex organs	ICD-O C 51 - 58
Peripheral nerves, autonomic nervous system	ICD-O C 47
Respiratory system, intrathoracic organs	ICD-O C 30 - 39
Retroperitoneum, peritoneum	ICD-O C 48
Skin	ICD-O C 44
Soft tissues	ICD-O C 49
Urinary organs	ICD-O C 67 - 68

Table 3: Example of tumour grouping for four selected groups.

Diagnosis group	Single diagnosis	Number	Percentage [%]

Skeletal tumour ICD-O 9180 - 9262	Adamantinoma of long bones	103	8.7
	Chondroblastoma	22	1.86
	Chondroma, fibrochondrosarcoma	168	14.19
	Osteochondroma	11	0.93
	Osteofibroma	38	3.21
	Osteoma, osteosarcoma	842	71.11
Total of skeletal tumours		**1,184**	**100**
Special gonadal neoplasia ICD-O 8610 - 8670	Granulosa cell tumour, granulosa cell carcinoma	93	8.72
	Leydig cell tumour	450	42.17
	Luteoma	9	0.84
	Sertoli cell adenoma, sertoli cell carcinoma	423	39.64
	Sertoli-Leydig cell tumour	92	8.62
Total of special gonadal neoplasia		1,067	100
Gonadal germ cell tumour ICD-O 9060-9085	Embryonal carcinoma	3	0.45
	Seminoma	632	95.47
	Teratoma	8	1.21
	Germ cell tumours	19	2.87
Total of germ cell tumours		**662**	**100**
Epithelial tumour ICD-O 8010 - 8587, ICD-O 9050-9058	Adenocarcinoma of anal glands	2,421	9.27
	Adenocarcinoma with squamous metaplasia	190	0.73
	Adenoma, Adenocarcinoma	12,348	47.27
	Adenomatous polyp, adenocarcinoma in adenomatous polyp	321	1.23
	Adrenal cortical adenoma, adrenal cortical adenocarinoma	168	0.64
	Basal cell carcinoma, adenoma	499	1.91
	Carcinoma, anaplastic type	296	1.13
	Cholangioma, cholangiocarcinoma	48	0.18
	Composite carcinoid	43	0.16
	Epithelial* tumour ICD-O 8010 – 9053	1,677	6.42
	Epithelioid mesothelioma	37	0.14
	Epithelioma	958	3.67
	Hepatoma, hepatocarcinoma	155	0.59

	Insulinoma	52	0.2
	Intracystic papillary adenoma, intracystic papillary adenocarcinoma	79	0.3
	Intraductal papilloma, intraductal papi	12	0.05
	Mesothelioma, biphasic, malignant	42	0.16
	Multifocal superficial basal cell carcinoma	231	0.88
	Papillary adenoma, adenocarcinoma	112	0.43
	Papillary carcinoma	871	3.33
	Pilomatrixoma	503	1.93
	Pulmonary adenomatosis, bronchiolo-alveolar adenocarcinoma	45	0.17
	Sebaceous adenoma, sebaceous adenocarcinoma	1,456	5.57
	Secretory carcinoma of the mammary gland	329	1.26
	Spindle cell carcinoma	72	0.28
	Squamous cell carcinoma	1,324	5.07
	Squamous papillomatosis	10	0.04
	Sweat gland adenoma, sweat gland adenocarcinoma	427	1.63
	Thymoma	96	0.37
	Transitional cell papilloma, transitional cell carcinoma	168	0.64
	Trichoepithelioma	1,132	4.33
Total of epithelial tumours		**26,122**	**100**

Table 4: The 17 most common canine breeds out of a total of 183 canine breeds among 121 963 canine patients.

Canine breed	Number	Percentage [%]
Shepherd	12,354	10.13%
Crossbreed	12,193	10.00%
Retriever	11,429	9.37%
Swiss Mountain Dog	7,774	6.37%
Poodle	7,214	5.91%
Dachshund	6,499	5.33%
Boxer	6,368	5.22%
Schnauzer	2,796	2.29%
Collie	2,206	1.81%
Yorkshire Terrier	2,157	1.77%
Cocker Spaniel	2,127	1.74%

Setter	2,105	1.73%
Great Dane	1,598	1.31%
Doberman Pinscher	1,596	1.31%
Rottweiler	1,470	1.21%
West Highland White Terrier	1,316	1.08%
Bulldog	1,016	0.83%
Parson Jack Russell Terrier	981	0.80%
Other breeds (including dogs of unknown breed)	38,764	31.78%
Total of all breeds	121,963	100%

Figure

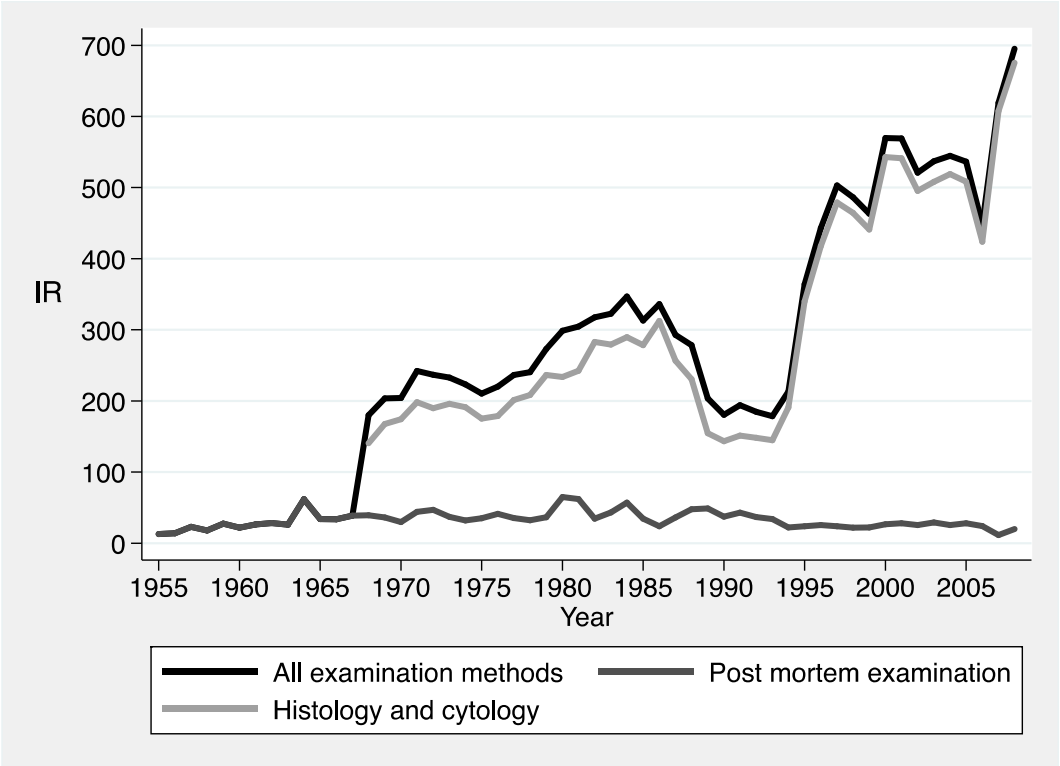

Figure 1: The influence of examination methods on the annual tumour incidence rate (IR = number of tumours diagnosed per 100 000 dogs in the Swiss dog population).

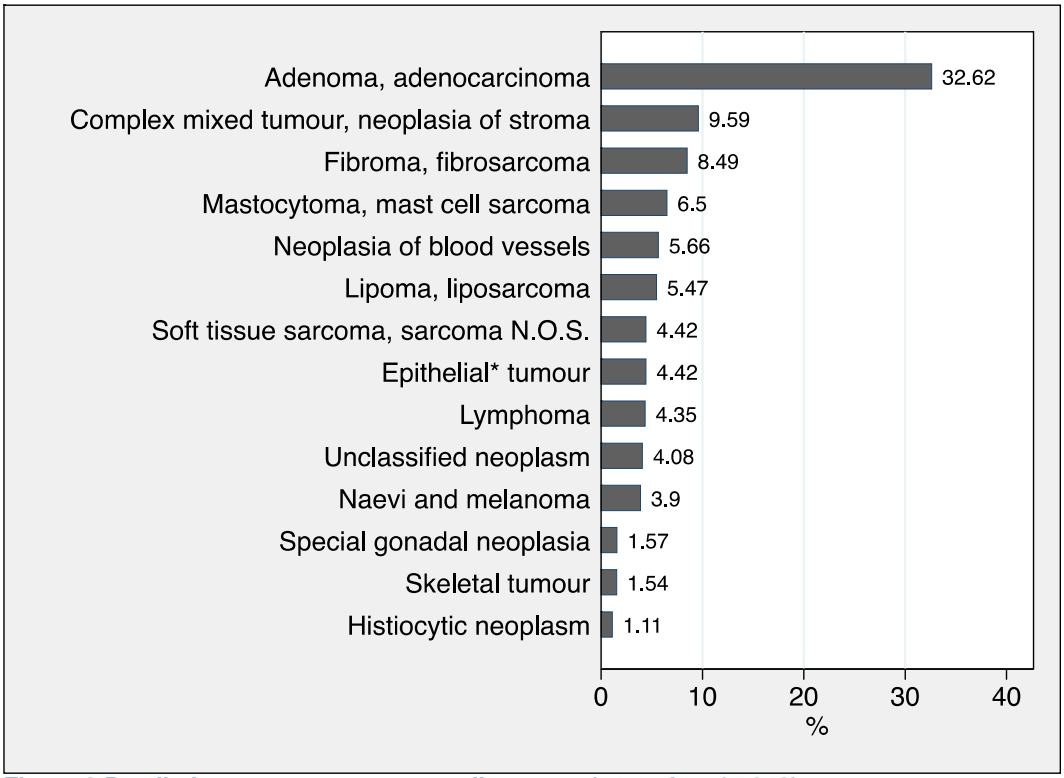

Figure 2 Detailed most common tumour diagnoses (>1% of n= 67 943).

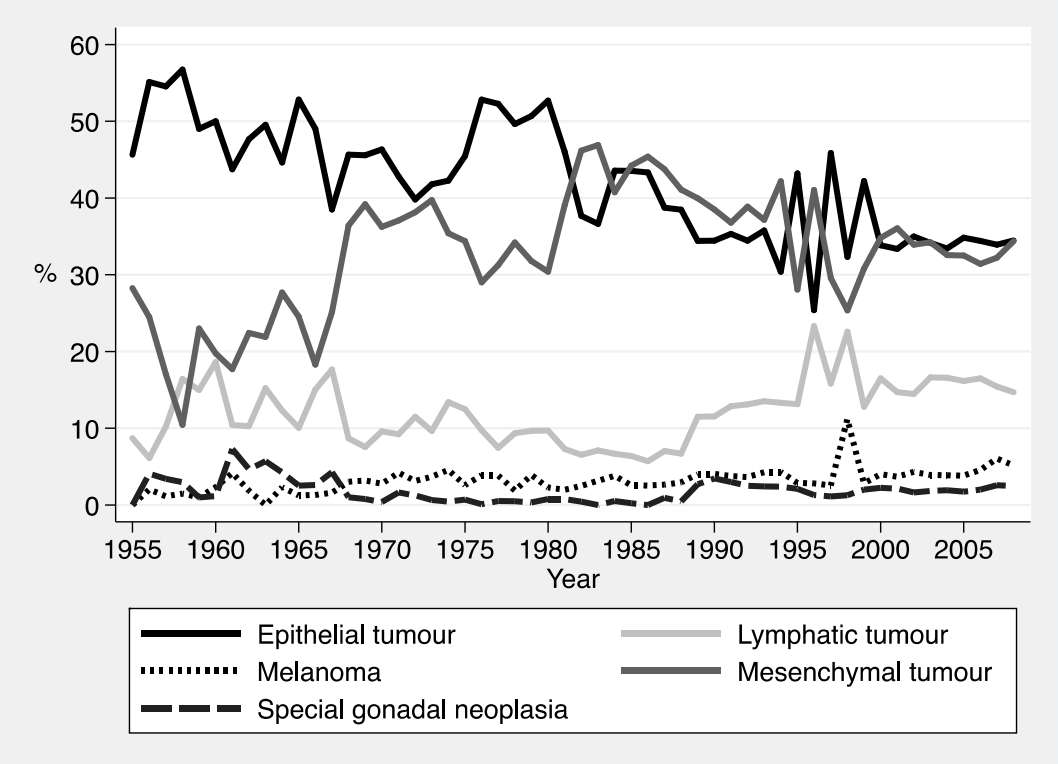

Figure 3: The yearly most prevalent tumour diagnoses. The percentage of a tumour type among all tumour types diagnosed per year.

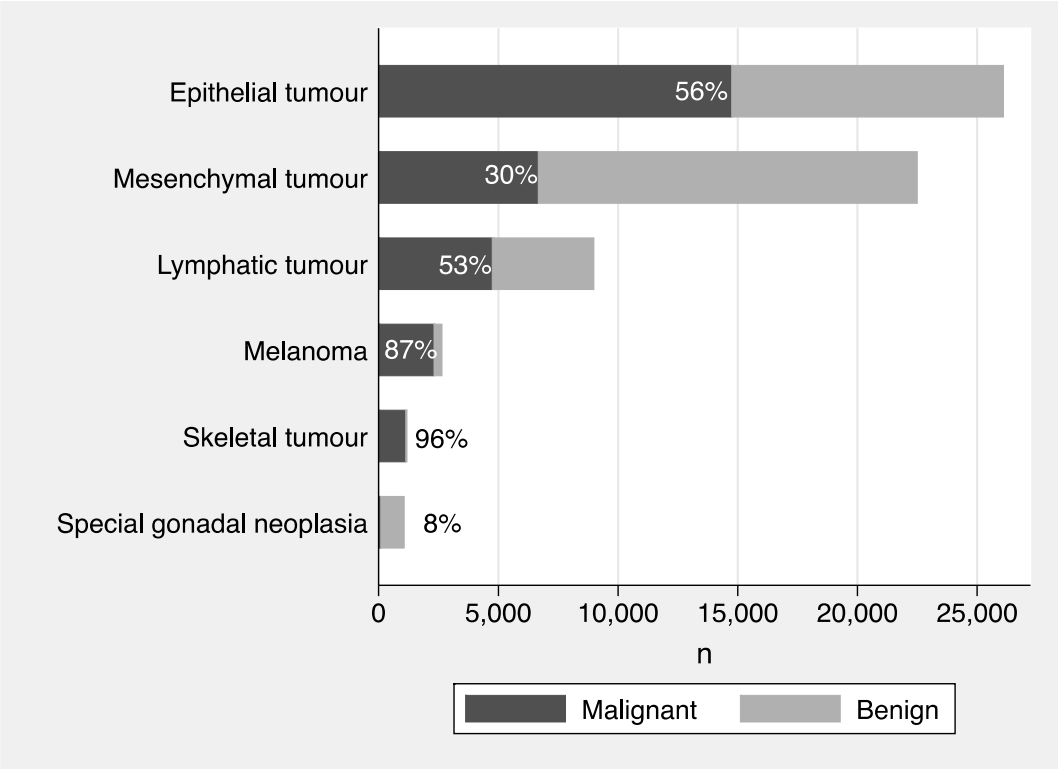

Figure 4: Absolute [n] and relative [%] distribution of the malignancy in tumour diagnoses. In this figure epithelial tumour includes ICD-O 8010 – 8587 and ICD-O 9050-9058.

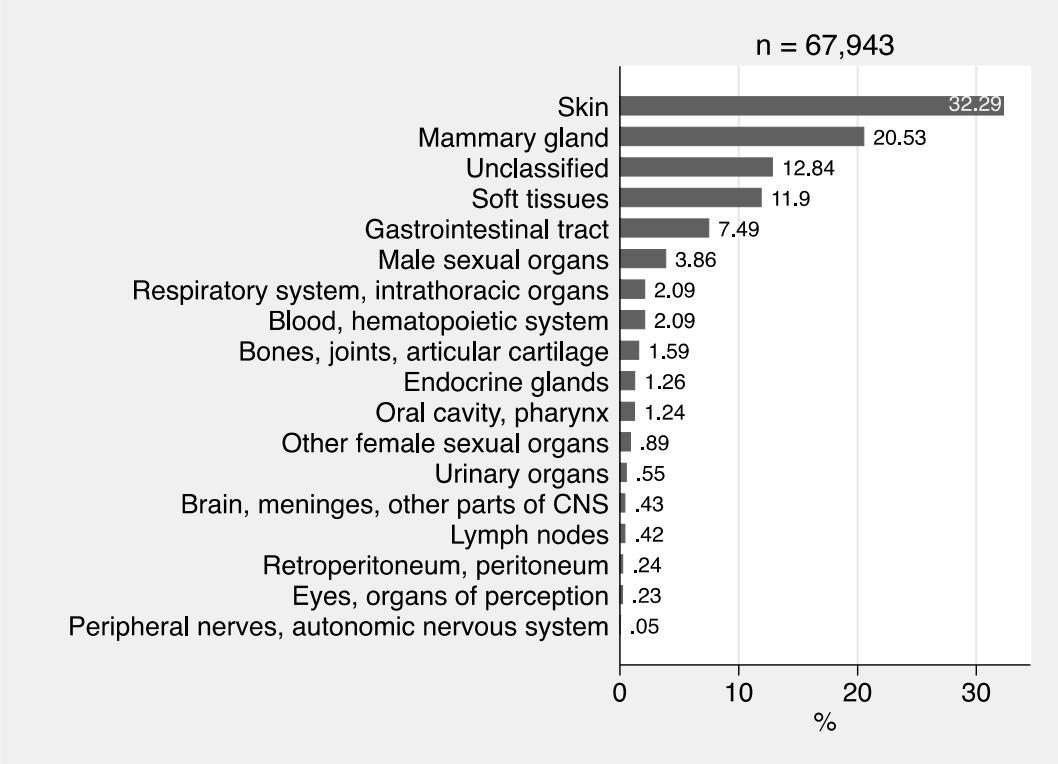

Figure 5: Distribution of tumour locations diagnosed by all examination methods. (n) = number of all samples. [%] = proportion of tumour location.

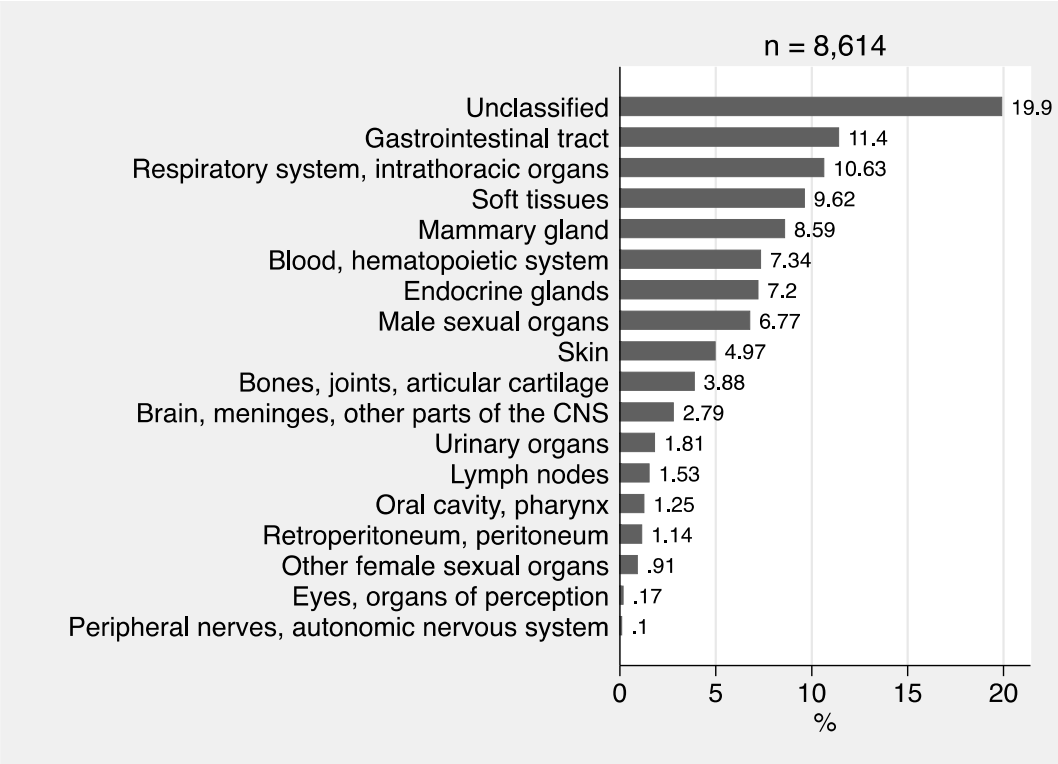

Figure 6: Distribution of tumour locations diagnosed by post mortem investigation. (n) = number of post-mortem samples. [%] = proportion of tumour location.

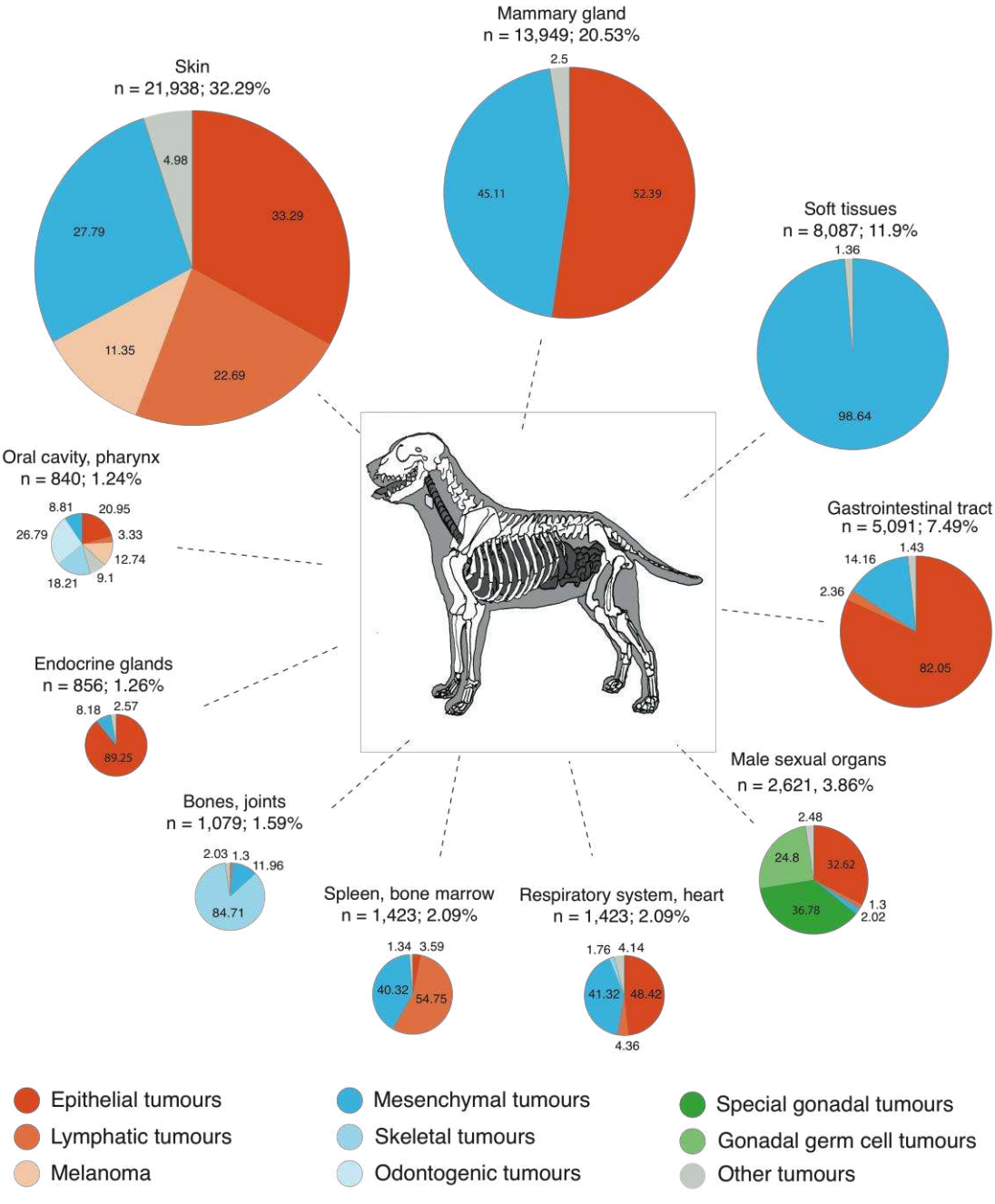

Figure 7: Tumour location and diagnoses. (n) = number of tumours found in a location; [%] = proportion of the location compared to the total of locations. Figures in and around the slices = relative proportion of tumour diagnoses / location. Tumour diagnoses lower than 1% were added into "Other tumours"; locations lower than 1% and unclassified location were not listed. With the exception of "male sexual organs" the listed locations are not sex specific.

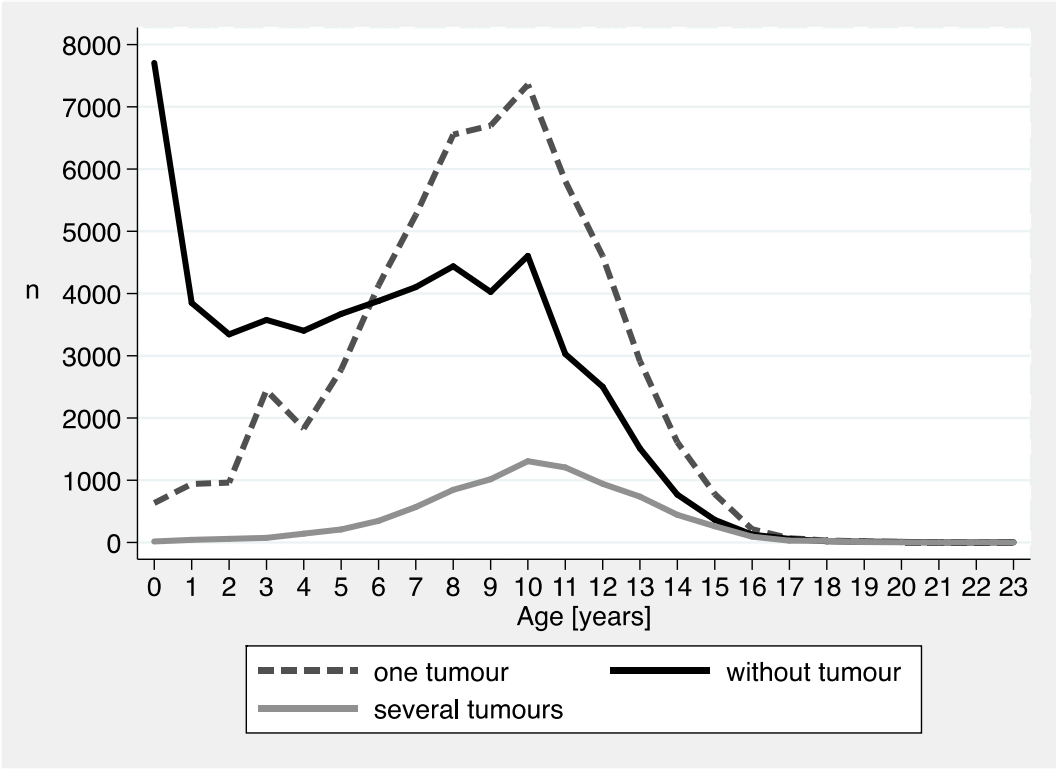

Figure 8: Canine patients with none, one or several tumours per age. (n) = number of patients.

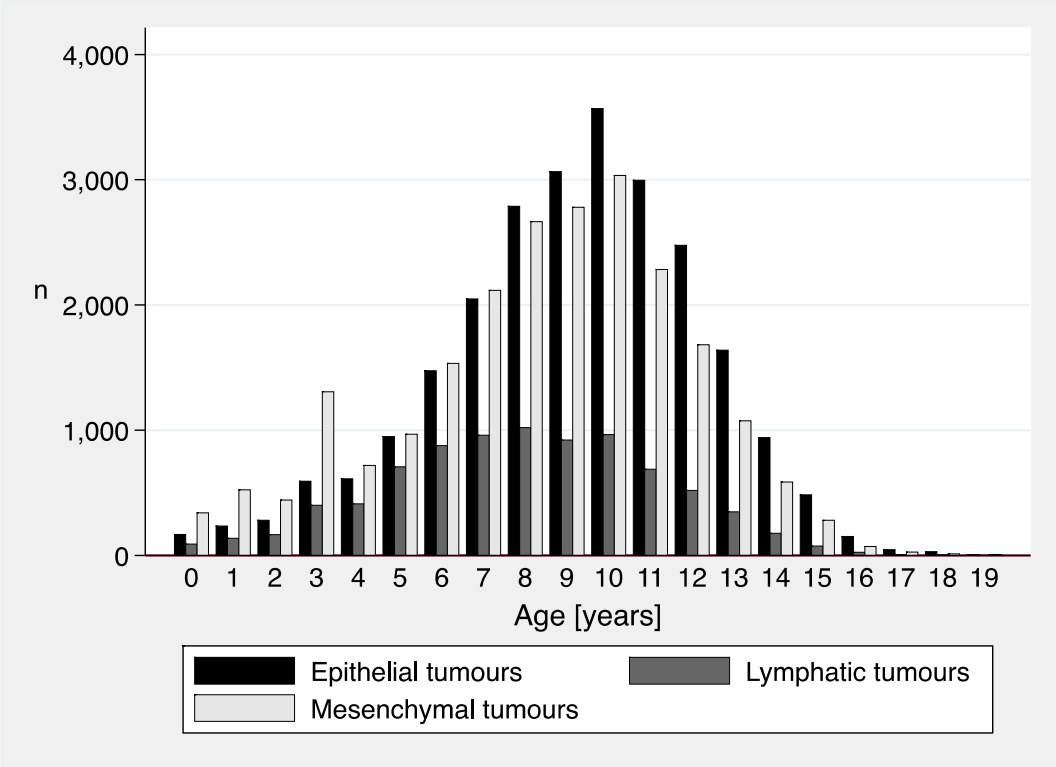

Figure 9: Epithelial, mesenchymal and lymphatic tumours per age of patient. n = number of tumour types per age.

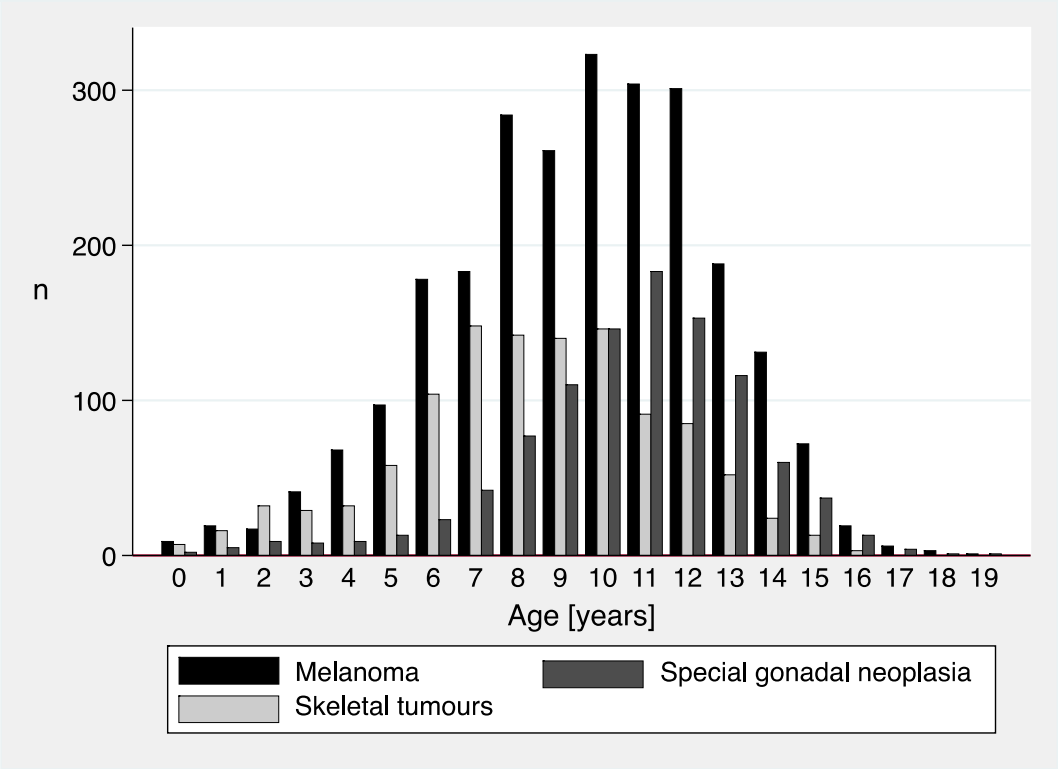

Figure 10: Melanoma, special gonadal neoplasia and skeletal tumours per age of patient. n = number of tumour types per age.